

In re Application of: Bier and Yu
Application No.: 09/215,569
Filing Date: December 16, 1998
Page 2 of 16

PATENT
Attorney Docket No.: 07349/019001
(041673-2007)

sub E1
D
F
The invention therefore provides Super-Sog (SEQ ID NO:2; amino acids 1-292 of Sog) and active variants thereof. Such variants include SEQ ID NO:4, a recombinant Super-Sog peptide which includes 33 amino acids encoded by the pUAS expression vector; SEQ ID NO:6, a Super-Sog peptide which includes a mutation (W→A) in the CR-1 sequence; and SEQ ID NO:8, a Super-Sog peptide which terminates 5' of the CR-1 sequence. Such variants also include Super-Sog with 5' modifications, such as modifications to the Tollid protease cleavage site, addition of other peptides and inclusion of additional 5' regions of Sog (e.g., CR-2).--

Please substitute the paragraph beginning at page 3, line 23, with the following replacement paragraph:

D2
FIGURE 1 is a diagram of the nucleotide sequence (SEQ ID NO:1) coding for a Super-Sog polypeptide, whose amino acid sequence (SEQ ID NO:2) is shown beneath the nucleotide codons in the Figure. Transmembrane (TM) and CR-1 regions of the coding sequence and peptide are indicated in the right margin of the FIGURE.--

Please substitute the paragraph beginning at page 3, line 28, with the following replacement paragraph:

73
FIGURE 2 is a compilation of the nucleotide sequence coding for a Super-Sog polypeptide and 33 amino acids encoded by the pUAS expression vector, coded by the nucleotide sequence following the NotI restriction site. The nucleotide sequence (SEQ ID NO:3) and the amino acid sequence (SEQ ID NO:4) are shown. --

Please substitute the paragraph beginning at page 4, line 1, with the following replacement paragraph:

In re Application of: Bier and Yu
Application No.: 09/215,569
Filing Date: December 16, 1998
Page 3 of 16

PATENT
Attorney Docket No.: 07349/019001
(041673-2007)

D4 ~~FIGURE 3 is the~~ nucleotide sequence (SEQ ID NO:5) coding for a Super-Sog peptide (SEQ ID NO:6) which includes a mutation (W→A) in the CR-1 sequence. --

Please substitute the paragraph beginning at page 4, line 5, with the following replacement paragraph:

D ~~FIGURE 4 is the~~ nucleotide sequence (SEQ ID NO:7) coding for a Super-Sog peptide which is modified 5' of the NotI restriction site sequence of SEQ ID NO:3 (SEQ ID NO:8). --

Please substitute the paragraph beginning at page 4, line 8, with the following replacement paragraph:

Dc ~~FIGURE 5 is a~~ line comparison demonstrating partial sequence homology between Super-Sog (SEQ ID NO:2) and another Dpp antagonist in *Drosophila*, noggin (SEQ ID NO:9). --

Please substitute the paragraph beginning at page 4, line 11, with the following replacement paragraph:

D ~~FIGURE 6 is the~~ full-length nucleotide sequence (SEQ ID NO:11) coding for wild-type Sog protein (SEQ ID NO:12). --

Please substitute the paragraph beginning at page 5, line 13, with the following replacement paragraph:

In re Application of: Bier and Yu
Application No.: 09/215,569
Filing Date: December 16, 1998
Page 4 of 16

PATENT
Attorney Docket No.: 07349/019001
(041673-2007)

D8
sub E27
-- Given their similarity in structure, it would be reasonably expected that any *Dpp* inhibitory activity conferred on the Sog protein by the CR repeats would be comparable in quality. It was therefore a surprise to find that a peptide encoded by CR-1 (Super-Sog; SEQ ID NO:2) has greater *Dpp* inhibitory activity in certain respects than wild-type Sog. --

Please substitute the paragraph beginning at page 6, line 16, with the following replacement paragraph:

D9
-- Super-Sog is prepared as a purified peptide fragment from Sog (e.g., SEQ ID NO:2), expressed as a recombinant peptide using, for example, the coding sequences set forth in SEQ ID NOs:1, 3, 5 or 7, or synthesized chemically. Techniques for production of peptides according to each of these methods are well-known in the art and so will only be described briefly here. --

Please substitute the paragraph beginning at page 7, line 14, with the following replacement paragraph:

D10
-- Recombinant Super-Sog can also be produced *in vitro* or *in vivo* through expression of a polynucleotide sequence which encodes Super-Sog (e.g., SEQ ID NO:1). In general, prokaryotes are used for cloning of DNA sequences in constructing recombinant expression vectors. For example, *E. coli* K12 strain 294 (ATCC Accession No. 31446) may be particularly useful. Prokaryotes also are used for expression. The aforementioned strain, as well as *E. coli* W3110 (ATCC Accession No. 27325), bacilli such as *Bacillus subtilis*, and other enterobacteriaceae such as *Salmonella typhimurium* or *Serratia marcescans*, and various *pseudomonas* species may also be used for expression. --

Please substitute the paragraph beginning at page 21, line 4, with the following replacement paragraph:

In re Application of: Bier and Yu
Application No.: 09/215,569
Filing Date: December 16, 1998
Page 5 of 16

PATENT
Attorney Docket No.: 07349/019001
(041673-2007)

-- SEQ ID NO:1 is the nucleotide sequence which codes for a Super-Sog polypeptide. --

N⁶ Please substitute the paragraph beginning at page 21, line 6, with the following replacement paragraph:

-- SEQ ID NO:2 is the predicted amino acid sequence of Super-Sog encoded by SEQ ID NO:1. --

N⁸ Please substitute the paragraph beginning at page 21, line 8, with the following replacement paragraph:

-- SEQ ID NO:3 is a compilation of the nucleotide sequence coding for a Super-Sog polypeptide and 33 amino acids of the pUAS expression vector, coded by the nucleotide sequence following NotI. --

N⁸ Please substitute the paragraph beginning at page 21, line 12, with the following replacement paragraph:

-- SEQ ID NO:4 is the predicted amino acid sequence encoded by SEQ ID NO:3. --

N⁸ Please substitute the paragraph beginning at page 21, line 15, with the following replacement paragraph:

-- SEQ ID NO:10 is a partial amino acid sequence for *noggin* encompassing a region of homology to *Super-Sog*. SEQ ID NO:9 is the full-length *noggin* amino acid sequence. --

In re Application of: Bier and Yu
Application No.: 09/215,569
Filing Date: December 16, 1998
Page 6 of 16

PATENT
Attorney Docket No.: 07349/019001
(041673-2007)

NE Please substitute the paragraph beginning at page 21, line 18, with the following replacement paragraph:

-- SEQ ID NO:5 is the nucleotide sequence coding for a Super-Sog peptide which includes a mutation (W→A) in the CR-1 sequence (SEQ ID NO:6). --

NE Please substitute the paragraph beginning at page 21, line 21, with the following replacement paragraph:

-- SEQ ID NO:7 is the nucleotide sequence coding for a Super-Sog peptide which is modified 5' of the NotI restriction site sequence of SEQ ID No:3 (SEQ ID NO:8). --

NE Please substitute the paragraph beginning at page 21, line 24, with the following replacement paragraph:

-- SEQ ID NO:11 is the full-length nucleotide sequence coding for wild-type Sog (SEQ ID NO:12). --